GGCTTCTCGTGGTTCCCAGAGCCCTGCTTAATGGATGGAGACCTGGACGAGAACCTGGCTGCTGTTGTTCT GAACATGGCCCAGAGCCCTGTGTCTGCCGAGGTCATTCACCAGGTGGAAGAGTGTCTTGATGAAGACGAG AAGGAGATGATGCTCTTCCTGTGTAGAGATGTGACTGAGAACCTGGCTGCACCTAACGTCAGGGACCTCC TGGATAGCTTAAGTGAGAGGCCAGCTCTCTTTTGCTACCTTGGCTGAATTGCTCTACAGAGTGAGGCG GTTTGACCTTCTCAAGAGGATCTTGAAGACAGACAAAGCAACCGTGGAGGACCACCTGCGCAGAAACCCT CACCTGGTTTCTGATTATAGGGTCCTGCTGATGGAGATTGGTGAGAGCTTAGATCAGAACGATGTATCCT CCTTAGTTTTCCTTACAAGGATTACAAGGGATTACACAGGCAGAGGCAAGATAGCCAAGGACAAGAGTTT CTTGGATCTGGTGATTGAATTGGAGAAACTGAATCTAATTGCTTCAGACCAATTGAATTTGTTAGAAAAA TGCCTGAAGAACATCCACAGAATAGACTTGAACACAAAGATCCAGAAGTACACCCAGTCCAGCCAAGGAG CAAGATCAAATATGAATACTCTCCAGGCTTCGCTCCCAAAATTGAGTATCAAGTATAACTCAAGGCTCCA GAATGGCCGAAGTAAAGAGCCAAGATTTGTGGAATACCGTGACAGTCAAAGAACACTGGTGAAGACATCC TAGGAATCTGCTTGATCATTGATTGTATTGGCAACGACAAAATATCTTCAAGAGACCTTCACTTCCCT GGGCTATCATATCCAGCTTTTCTTGTTTCCCAAGTCACATGACATAACCCAGATTGTTCGCCGATATGCA AGTATGGCCCAACATCAAGACTATGACAGCTTTGCATGTGTTCTGGTGAGCCTAGGAGGCTCCCAAAGCA TGATGGGCAGAGATCAAGTTCACTCAGGGTTCTCCTTGGATCATGTCAAGAACATGTTCACGGGGGACAC GAAGATAGCAGCCTGGAGGTAGATGGGCCATCAATAAAAAATGTGGACTCTAAGCCCCTGCAACCCAGAC ACTGCACAACTCACCCAGAAGCTGATATCTTTTGGAGCCTGTGCACAGCAGACGTATCTCACTTGGAGAA GCCCTCCAGCTCATCCTCTGTGTATCTGCAGAAGCTCTCCCAGCAGCTGAAGCAAGGCAGGAGACGCCCA CTCGTGGACCTCCACGTTGAACTCATGGACAAAGTGTATGCGTGGAACAGTGGTGTTTCGTCTAAGGAGA AATACAGCCTCAGCCTGCAGCACACTCTGAGGAAGAACTCATCCTGGCTCCTACGTGAGAACCCCAGAC GCTGCTTCTGCCTTGAGTCCTGGCCTAGGGTTCTCCTGTGCACAGGCATGAGCCGTAACCCTGT GCCTGGGAAACGTCTCACTCCCGCCGCGCGTGCCTTTACCTCTCTAAACTTCCCTACTTACATTCCTTAGT GGTTATCTACCAAGTTATACCAAGTTATTGTATGGGTGTATAGTGTATAGTGGTTCAAGATTCTGAATGT AACTTGAGACTTACCTGAGTTTGTCATGCGACTGGGTAAATTGTTTCTATGGCACATCTAATCATTTAAT AAGTAATTACCTCATTAAGTACCCATTGCTTCAGGACTTTCACATTGGCCACCAATTTCTGTGACCCAGC TCCACATTTATATTCTCTTTCGGCAAAACCAAATTTCATTATGTCTGTTTAATATCTACAGTCTAATGCT TTGTAAGACATCTAGATAGGAAAAATAGTTACCCATGAGCACAGGAGGGCTGGCCTGACCCTCACCAGCTG $\tt TGCAGTGGCTTCGGTGAAAGGAGAATGAGCCCTACTCCTTGAAAGGTTGTAGTGCTTGGGAGAGCAGTCT$ $\tt TTGGCTCAGGATCAGGAACAGGAGGGATGACCAACTTGGGGCTTTGAGGTGGCCCACCCCAGCATCCAT$ ATCATCTGTGAACTGCCAGAGCCTGTGAAGGGGCGGGTCCTGTAGAACTAAGGCTGCAGGATCTCCATGA CACAGGGCAACAACAGGGTATCTGAGAAGGGTCCCCGTGAGGGTCCAGTATTTATAGTGCACCAGAAGCC AGAGGCCTCGGATCAGACAATGACCCATTGCACTGAGTAAAGATGTAAGTGAATGAGTGAAGATGTGTGG GGTGCATGATATAGAATTCACAAAGAAAAAAAAAAAAA (SEQ ID NO:1)

MAQSPVSAEVIHQVEECLDEDEKEMMLFLCRDVTENLAAPNVRDLLDSLSERGQLSFATLAELLYRVRRFDLLKRILKTDKATVED HLRRNPHLVSDYRVLLMEIGESLDQNDVSSLVFLTRITRDYTGRGKIAKDKSFLDLVIELEKLNLIASDQLNLLEKCLKNIHRIDL NTKIQKYTQSSQGARSNMNTLQASLPKLSIKYNSRLQNGRSKEPRFVEYRDSQRTLVKTSIQESGAFLPPHIREETYRMQSKPLGI CLIIDCIGNDTKYLQETFTSLGYHIQLFLFPKSHDITQIVRRYASMAQHQDYDSFACVLVSLGGSQSMMGRDQVHSGFSLDHVKNM FTGDTCPSLRGKPKLFFIQNYESLGSQLEDSSLEVDGPSIKNVDSKPLQPRHCTTHPEADIFWSLCTADVSHLEKPSSSSSVYLQK LSQQLKQGRRRPLVDLHVELMDKVYAWNSGVSSKEKYSLSLQHTLRKKLILAPT (SEQ ID NO:2)

FIGURE 1

<u>underlined</u> = deleted in targeting construct

[] = sequence flanking Neo insert in targeting construct

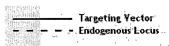
[GGCTTCTCGTGGTTCCCAGAGCCCTGCTTAATGGATGGAGACTGGACGAGAACCTGGCTG CTGTGGTTCTGAACATGGCCCAGAG] CCCTGTGTCTGCCGAGGTCATTCACCAGGTGGAAG **AGTGTCTTGATGAAGACGAGAAGGAGATGATGCTCTTCCTGTGTAGAGATGTGACTGAGA** <u>ACCTGGCTGCACCTAACGTCAGGGACCTCCTGGATAGCTTAAGTGAGAGAGGCCAGCTCT</u> CTTTTGCTAC [CTTGGCTGAATTGCTCTACAGAGTGAGGCGGTTTGACCTTCTCAAGAGGA TCTTGAAGACAGACAAAGCAACCGTGGAGGACCACCTGCGCAGAAACCCTCACCTGGTTT CTGATTATAG] GGTCCTGCTGATGGAGATTGGTGAGAGCTTAGATCAGAACGATGTATCCT CCTTAGTTTTCCTTACAAGGATTACAAGGGATTACACAGGCAGAGGCAAGATAGCCAAGG ACAAGAGTTTCTTGGATCTGGTGATTGAATTGGAGAAACTGAATCTAATTGCTTCAGACC AATTGAATTTGTTAGAAAAATGCCTGAAGAACATCCACAGAATAGACTTGAACACAAAGA TCCAGAAGTACACCCAGTCCAGCCAAGGAGCAAGATCAAATATGAATACTCTCCAGGCTT CGCTCCCAAAATTGAGTATCAAGTATAACTCAAGGCTCCAGAATGGGCGAAGTAAAGAGC CAGGAGCTTTTTTACCTCCGCACATCCGTGAAGAGACTTACAGGATGCAGAGCAAGCCCC TAGGAATCTGCTTGATCATTGATTGTATTGGCAACGACAAAATATCTTCAAGAGACCT TCACTTCCCTGGGCTATCATATCCAGCTTTTCTTGTTTCCCAAGTCACATGACATAACCC AGATTGTTCGCCGATATGCAAGTATGGCCCAACATCAAGACTATGACAGCTTTGCATGTG TTCTGGTGAGCCTAGGAGGCTCCCAAAGCATGATGGGCAGAGATCAAGTTCACTCAGGGT TCTCCTTGGATCATGTCAAGAACATGTTCACGGGGGACACGTGCCCTTCTCTCAGAGGGA AGCCAAAGCTCTTTTTTATTCAGAACTATGAGTCGTTAGGTAGCCAGTTGGAAGATAGCA GCCTGGAGGTAGATGGGCCATCAATAAAAAATGTGGACTCTAAGCCCCTGCAACCCAGAC ACTGCACAACTCACCCAGAAGCTGATATCTTTTGGAGCCTGTGCACAGCAGACGTATCTC ACTTGGAGAAGCCCTCCAGCTCATCCTCTGTGTATCTGCAGAAGCTCTCCCAGCAGCTGA AGCAAGGCAGGAGACGCCCACTCGTGGACCTCCACGTTGAACTCATGGACAAAGTGTATG CGTGGAACAGTGGTGTTTCGTCTAAGGAGAAATACAGCCTCAGCCTGCAGCACACTCTGA GGAAGAACTCATCCTGGCTCCTACGTGAGAACCCCAGACCGTTGGTGTTCTTGGTATAT CATCCAGGGTGGCGGCTTGGAGCAGAGCTTGGCGGTTACGGCTGCTTCTGGCTGCTTCTG GCTCTGCCGTGAGTCCTGGCCTAGGGTTCTCCTGTGCACAGGCATGAGCCGTAACCCTGT GCCTGGGAAACGTCTCACTCCCGCCGCCGTGCCTTTACCTCTCTAAACTTCCCTACTTAC ATTCCTTAGTCGGATGTTTTGCCAGAGTGTGGAGAACAGTAAGACATAAACCTATTGTTT GTTTGTTTTTTGGGGGGGGGGTTATCTACCAAGTTATACCAAGTTATTGTATGGGTGTA TAGTGTATAGTGGTTCAAGATTCTGAATGTAACTTGAGACTTACCTGAGTTTGTCATGCG ACTGGGTAAATTGTTTCTATGGCACATCTAATCATTTAATAAGTAATTACCTCATTAAGT ACCCATTGCTTCAGGACTTTCACATTGGCCACCAATTTCTGTGACCCAGCTCCACATTTA TATTCTCTTTCGGCAAAACCAAATTTCATTATGTCTGTTTAATATCTACAGTCTAATGCT TTGTAAGACATCTAGATAGGAAAAATAGTTACCCATGAGCACAGGAGGGCTGGCCTGACC $\mathtt{CTCACCAGCTGTGCAGTGGCTTCGGTGAAAGGAGAATGAGCCCTACTCCTTGAAAGGTTG}$ ACACAACAGTGAGTGGGGGAGCTTGCCCTGGTTGGCTCAGGATCAGGAAACAGGAGGGAT GACCAACTTGGGGCTTTGAGGTGGCCCACCCCAGCATCCATATCATCTGTGAACTGCCAG AGCCTGTGAAGGGGCGGGTCCTGTAGAACTAAGGCTGCAGGATCTCCATGACACAGGGCA ACAACAGGGTATCTGAGAAGGGTCCCCGTGAGGGTCCAGTATTTATAGTGCACCAGAAGC CAGAGGCCTCGGATCAGACAATGACCCATTGCACTGAGTAAAGATGTAAGTGAATGAGTG TTTGTTTGTTTGTTTTTTTTTTTTTGGCAGGAACAGATTGCAAGGGCAGAGAGTA GATAAGGAAGCTGGAGACATGAGTGGGGTTGGGTGCATGATATAGAATTCACAAAGAAAA AAAAAAAAA



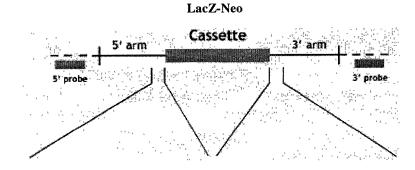
Targeting Vector* (genomic sequence)

Construct Number: 3547

Arm Length: 5': 0.3 kb 3': 4.8 kb



* Not drawn to scale



5'>CCTGTGCTTTGACTCTCAAGC CTAAGTGTTTTGATAAGAGGATTC TCTTTCACCACAGAGTGTCTCTAT TGCAAGAACTCTGAGAGAAATGAA GAGAGTCCTCAGCAATGATGTTGG CTTCTCGTGGTTCCCAGAGCCCTG CTTAATGGATGGAGACTGGACGAG AACCTGGCTGCTGTGGTTCTGAAC ATGGCCCAGAG<3'(SEQ ID NO:3) 5'>CTTGGCTGAATTGCTCTACAG AGTGAGGCGGTTTGACCTTCTCAA GAGGATCTTGAAGACAGACAAAGC AACCGTGGAGGACCACCTGCGCAG AAACCCTCACCTGGTTTCTGATTA TAGGTAAGTCATCCCCTGGGGGAG GGGAGAGGGAGTCTAGATGGTTAG GGCAGTGAGAAGACCCCATTGCTT CCTCTTCTCTC<3'(SEQ ID NO:4)

250 bp



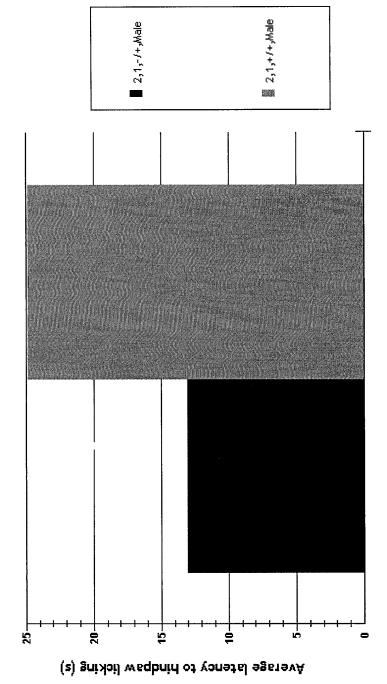


FIGURE 3



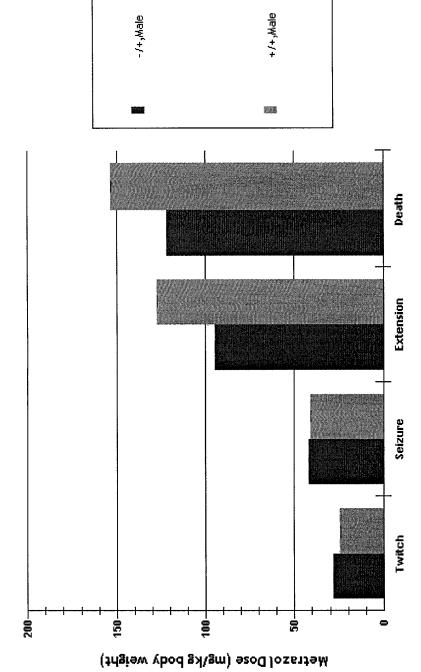


FIGURE 4